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Subject: Environmental Defense comments on Dimethyl Sulfoxide (CAS# 67-68-5)

(Submitted via Internet 2/29/04 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and ehunt@adelphia.net)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for Dimethyl Sulfoxide (CAS# 67-68-5).

The documents on dimethyl sulfoxide (DMSO) were submitted by the Dimethyl Sulfoxide Producers Association. The submission did not contain a test plan but fortunately, the robust summaries were very complete. The lack of a test plan makes the submission not user-friendly and certainly difficult to evaluate. We urge the sponsor to submit a formal test plan.

The only information on uses of DMSO were found in the cover letter, which states that DMSO is used in a wide variety of applications, including as a reaction solvent for industrial syntheses; in antifreeze, hydraulic fluids, and cleanup solvents; and in the manufacture of synthetic fibers and pesticides. It is also used as a pharmaceutical solvent, medicinal treatment and as an aid for penetration of dermally administered drugs. Based on these uses, there is ample opportunity for both environmental and human exposures and a separate test plan is warranted. We also request that the sponsor provide any data on environmental monitoring and human exposures from different sources.

The sponsor claims that available studies are adequate to fulfill SIDS endpoints. After wading through the 133 pages of robust summaries, we agree. The available data on DMSO are extraordinarily rich, with studies that go beyond HPV requirements in many cases, and the studies are well-described in the robust summaries.

Specific comments are as follows:

1. There are multiple studies on aquatic toxicology endpoints and they all demonstrate that DMSO has low toxicity for fish, aquatic invertebrates and plants.

2. Pharmacokinetic studies in experimental animals and people demonstrate that the major metabolite of DMSO is dimethylsulfone. This metabolite does not appear to have different toxicological properties than DMSO.

3. DMSO has very low toxicity as evidenced by data from all mammalian health endpoints, often obtained from several species using multiple routes

of exposure; the LD50 is approximately 20 mg/kg and the repeat dose NOEL is approximately 1g/kg, with ocular toxicity as the most consistent and sensitive endpoint.

4. There are several developmental toxicology studies in rodents and frogs and they all demonstrate that DMSO has little developmental toxicity. The fertility studies are methodologically weak, but the wealth of data from the repeat dose and developmental toxicity studies are sufficient to conclude that DMSO possesses little or no reproductive toxicity.

5. A wide array of genetic toxicity tests are generally negative, although one study showed evidence of chromatid breaks in rats. Detailed methodological information is provided, although the year of the study is not indicated. Does the sponsor have an explanation for why this study was positive and other in vivo genetic tests negative?

Thank you for this opportunity to comment.

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